IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Miri Seiberg et al.	Attorney Docket No.: JBP-438
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Filed :	December 7, 1998	Examiner: Michael V. Meller
For :	METHODS FOR REGULATING PHAGOCYTOSIS AND ICAM-1 EXPRESSION	

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June 18, 2009
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Commissioner for Patents
Alexandria, VA 22313-1450

REPLY BRIEF

This Reply Brief is respectfully submitted in response to the Examiner's Answer of May 19, 2009.

i. Withdrawn Rejection

Appellants note with gratitude the withdrawal of the rejection of claims 75-84 under 35 U.S.C. 102(a) as being anticipated by JP Patent No. 410226642.

ii. Reply to Examiner's Answer

Claims 75-84 remain rejected under 35 U.S.C. 102(b) as being anticipated by JP 408143442 (hereinafter referred to as "Matsuura").

Appellants maintain their position that the rejection of Claims 75-84 under 35 U.S.C. §102(b) as being anticipated by JP Patent Application No. Hei-8-143442 to Matsuura et al (JP '442) (hereinafter, "Matsuura" or "JP '442") is improper and without basis and should be overruled.

Matsuura relates to "…an external preparation for skin blended with a water extract liquid of soybeans…" [Matsuura, p. 3, ¶0001]. Matsuura is centered on obtaining soybean extracts that contain glycosides, i.e., soluble sugars: "…it has been confirmed that a glycoside in a soybean has various physiological actions." [Matsuura, p. 4, ¶0002]. Matsuura also refers to "the case where this soaked liquid is concentrated, concentration under reduced pressure is carried out…in such a manner that the ***soluble sugar content*** is in the range of 10 to 50 g/100 ml." [Matsuura, p. 7, ¶0008] (emphasis added)

Matsuura clearly states that the inventors:

> …focused attention on a soaked liquid of soybeans, ***which is generated as a by-product during the production of tofu, and conducted studies for aiming at making efficient use of the soaked liquid***…they found that a filtrate generated as a ***by-product during the ultrafiltration concentration of soymilk*** and whey generated during the product of a soy protein isolate also have a similar effect. [Matsuura, p. 4, ¶0003] (emphasis added)

This would indicate that Matsuura was concerned with finding uses for the by-products of ingestible food and drink products.

Appellants respectfully submit that, while claims 5 and 6 of Matsuura purport to describe very broad processes of obtaining soybean extracts, these claims are aspirational, rather than instructive to those of ordinary skill in the art. Appellants respectfully contend

that the claims must be read and understood in their entirety and in the context of the entire publication as well as in the context of the understanding of those of ordinary skill in the art at the time the invention herein was made.

a. Matsuura Nowhere Explicitly Describes or Recognizes the Presence of STI

The Examiner's Answer first replies to appellants' statement that nowhere does Matsuura mention that the soybean extracts described therein contain active soy trypsin inhibitor proteins, stating that:

> Since STI are in soybeans and since the soybeans are not required to be heated to a temperature which would denature them (see claim 5 of JP '442 then it would have been inherent that the STI are in the extract of JP '442. Further as noted on page 16 of the instant specification, appellants admit that soybean milk contains STI which is clearly claim by JP '442, see claim 6 of JP '442.[Examiner's Answer, pp. 4-5]

Appellants respectfully submit that, indeed, Matsuura ***never*** mentions or recognizes the presence of active soy trypsin inhibitory (hereinafter "STI") proteins in the compositions described therein. Matsuura's reference to utilizing the "soaked liquid of soybeans, which is generated as a by-product during the production of tofu" [Matsuura, p. 4, ¶0003] as well as the reference to the "by-prdouct during the ultrafiltration concentration of soymilk and whey" [Matsuura, p. 4, ¶0003] clearly refers to materials that have been processed in such a way as to be acceptable as ingestible food products. One of ordinary skill in the art, as has been established previously during the course of the prosecution of this application, would have understood that ingestible food products must not contain active STI. [Declaration of Katharine Martin, dated February 8, 2002, ¶¶4, 5].

In reviewing the examples set forth in the Matsuura publication, the processes described therein that are required to make the preparations described all require either the dehulling or defatting of the soybeans [Matsuura, ¶¶0007, 0012, 0020, 0021], both of which processes would include heat and/or organic extraction, and would denature STI. [Declaration of Katharine Martin, ¶¶4, 5; Declaration of Miri Seiberg, July 30, 2008, ¶3]

Although the soaking of whole soybeans is described in very general terms, Matsuura indicates that the soaking liquid is subjected to higher temperatures (i.e., 45 to 65°C) to concentrate the soluble sugar content therein. [Matsuura, p. 7, ¶0008]

Furthermore, Matsuura, even in claims 5 and 6, treats preparations derived from "whole soybeans", "dehulled soybeans" and "defatted soybeans" in the same way and ***never*** distinguishes among such preparations to indicate that active soy trypsin inhibitors must be preserved in order to obtain activity in skin care preparations.

b. Kunitz et al. Is Pertinent Vis-à-vis Diffusion of STI

The Examiner's Answer further addresses the Declaration of Miri Seiberg and the Kunitz et al. article. The Examiner's Answer states that:

> The declaration of Dr. Seiberg is referring to Table VI (page 305) of Kunitz which clearly is concerned with the chemical and physical properties of **crystalline** soybean trypsin inhibitor. Note also that the diffusion coefficient that Dr. Seiberg references only applies at 24°C.
>
> The instant claims and JP '442 are not dealing with **crystalline** soybean trypsin inhibitor. The enzyme trypsin has been **crystallized** in Kunitz but not in the instant invention or in JP '442. Further, only at 24°C is the diffusion coefficient even valid. Thus, since the same STI is not even being compared since the instantly claimed STI and that of JP '442 are not crystalline then Kunitz is not even a valid reference for support from the Seiberg declaration thus making the Seiberg declaration invalid and inoperative as a declaration for appellant.
>
> Further, it is noted in claim 6 of JP '442 that the soybeans are ground thus making it inevitable that an effective amount of STI will diffuse from the soybeans into the soaking liquid in which it resides. [Examiner's Answer, p. 5]

Appellants respectfully submit that this rebuttal is based upon the broad assumptions that (a) crystalline soybean trypsin inhibitor protein is not present in either the compositions of appellant's invention or in Matsuura; (b) crystalline soybean trypsin inhibitor protein would have a different diffusion rate than non-crystalline soybean trypsin inhibitor and (c) the diffusion rate of soybean trypsin inhibitor protein would change with temperature and that considering the diffusion rate of soybean trypsin inhibitor protein at 24°C would not be sufficient to extrapolate the diffusion behavior of soybean trypsin inhibitor at other temperatures.

Appellants respectfully contend that there is much value in the Declaration of Miri Seiberg relating to the Kunitz et al. publication and the diffusion rate of STI proteins set forth therein. Whether or not soybean trypsin inhibitor protein is present in the soybeans of Matsuura in crystalline form or non-crystalline form, the Kunitz et al. publication and Dr. Seiberg's Declaration conclude that the diffusion rate of such a protein is ***extremely slow***. As a large molecule, it is difficult for a protein to move through cell walls and plant structures. Even if the diffusion rate changes with temperature, the rate at 24°C exemplified in Kunitz et al., which is approximately room temperature, is still extremely slow. Because molecules move more slowly at lower

temperatures, one would conclude that the diffusion rate would be considerably slower at 5ºC, for example. Even Matsuura states as follows in reference to soaking periods for obtaining soluble sugars, the desired component in the Matsuura compositions:

> …in the case where soaked soybeans are used as a raw material for tofu or the like, it is necessary to consider the elution of proteins. Therefore, as preferred conditions, soaking is carried out at 20 to 30ºC for 8 to 20 hours, at 40 to 55ºC for 1 to 6 hours or 70 to 90ºC for 5 to 30 minutes. After the soaking, separation into soybeans and soaked liquid is carried out, and this soaked liquid is used as a raw material. [Matsuura, pp. 6-7, ¶0008]

Thus, Matsuura indicates that at temperatures such as that set forth in Kunitz et al., long periods of soaking to obtain the desired "soluble sugar content" is desired. [Matsuura, p. 7, ¶0008] It should be noted that it is well-known that glycosides (or soluble sugars), the molecules of stated interest in the Matsuura publication, are of much smaller molecular weight, and have much better solubility properties (hence the appellation, "***soluble*** sugar") than large protein molecules such as STI proteins. At lower temperatures, such as 5ºC, appellants respectfully submit that it would be highly unlikely for STI proteins to appear in the soaking water of Matsuura, even if soluble sugars may appear.

Appellants respectfully submit, in light of the foregoing discussion, that their reliance upon the Declaration of Miri Seiberg and the Kunitz et al. reference is appropriate.

c. Matsuura's Temperature Range of 5-100ºC Does Not Teach the Compositions and Methods of Appellants' Invention

The Examiner's Answer addresses the argument that the soaked soybean material in Matsuura is subjected to high heat. The Examiner's Answer acknowledges that exposure to high heat denatures proteins such as STI [Examiner's Answer, p. 6]. However, the Answer further notes as follows:

> …claim 5 clearly indicates that the soybeans are heated at 5-100ºC for 5 minutes. Thus, the portion that Dr. Zivin is referring to is only one embodiment of the claimed invention of JP '442. Clearly JP '442 encompasses more than just the temperatures recited by Dr. Zivin such as 20-30ºC which would not denature

> the STI, see pages 6-7 of the translation, paragraphs 8 and 9. [Examiner's Answer, p. 6]

Appellants respectfully contend that one of ordinary skill in the art at the time their invention was made would not have learned how to make the compositions of their invention based upon the wide range of temperatures set forth in claim 5 of Matsuura. In fact, this wide range could be considered misleading and confusing to those of ordinary skill in the art.

The range of 5-100ºC encompasses temperatures from 41ºF to 212ºF, the boiling temperature of water, on the Fahrenheit scale. In fact, 5ºC, or 41ºF, is considerably lower than normal ambient room temperature, which would require the ***lowering*** of the temperature of raw soybean material on which the processes set forth in Matsuura operate. Matsuura characterizes water having a temperature of 5ºC as "cold water" [Matsuura, p. 9, ¶0012]. This wide range of temperatures in the claim could be read as an attempt by Matsuura to cover a broad range of operating temperatures, rather than an actual teaching of how to make the compositions described therein.

Indeed, the temperature ranges set forth in Matsuura's examples are considerably higher than 5ºC: In Example 1, the whole soybeans are subjected to 75 ºC heat during the process of dehulling, mashed in water having a temperature of 5ºC, then heated at 100ºC and finally subjected to "thermal sterilization at 120ºC for 3 minutes" [Matsuura, p. 9, ¶0012]. The soybean materials of Example 2 were similarly dehulled and treated with hot air. [Matsuura, p. 12, ¶0020] The soybean materials of Example 3 were derived from defatted soybean flakes. [Matsuura, p. 13, ¶0021] Defatting, as set forth in Example 4 of Matsuura at p. 13, ¶0022, requires exposure to hexane, an organic solvent. The soybeans of Example 4 were also exposed to 75ºC hot air. Exposure to organic solvents and high temperatures are both processes which denature the soy trypsin inhibitory proteins in the beans. [Declaration of Miri Seiberg of July 30, 2008, ¶3, Declaration of Katharine Martin, ¶¶4, 5].

The soybeans materials of claim 5 (the only claim in which the temperature range is given as 5-100ºC) are either "whole soybeans", which, as discussed above, will not

enable the diffusion of STI into the soaking water, or "dehulled" or "defatted" soybeans, which are processed with heat and/or organic extraction.

Thus, despite the wide range of process temperatures set forth in claim 5, a full and careful reading of the Matsuura text reveals that the use of "cold water" takes place during only a small portion of the process. Matsuura teaches treating the raw soybean materials with a wide range of temperature and/or solvents during the course of the preparation process ***in addition*** to any exposure to the bottom of the range of temperatures. It cannot be assumed from reading claim 5 alone, and out of the context of the remainder of the publication, that the process described therein would ***inevitably*** result in a non-denatured soy trypsin inhibitor protein-containing soy extract.

d. The Process of Claim 6 Must Be Read In the Context of the Matsuura Text

The Examiner's Answer further addresses the point that "even if the STI remained intact in the soybeans throughout the processing steps described therein, it would not be present in the compositions that JP '442 describes." [Examiner's Answer, p. 6] The Examiner's Answer indicates in response that "…claim 6 makes it clear that the preparation is made by **grinding whole soybeans, dehulled soybeans or defatted soybeans** thus making it clear that the soybean was ground making the STI available for diffusion into the water." [Examiner's Answer, p. 6]

In response to the point set forth in the Examiner's Answer, appellants respectfully submit that the process set forth in Claim 6 of Matsuura must be read as a whole as well as in the context of the entire document. Claim 6 reads as follows:

> [Claim 6] A process for producing an external preparation for skin characterized by grinding whole soybeans, dehulled soybeans or defatted soybeans while adding water thereto, ***filtering the ground matter after it is heated***, filtering the obtained soymilk with an ultrafiltration membrane, and to the resulting filtrate as such or after it is concentrated, adding any of a variety of bases, fragrances, colorants and the like and mixing them. [Matsuura, p. 3, claim 6] (emphasis added)

Regardless of the type of the raw material used, Matsuura indicates that a filtering step takes place on "the ground material ***after*** it is heated" [Matsuura, p. 3, claim 6] (emphasis added). Claim 6, therefore, requires heating for the next step of the process, after soaking. This requirement is in consonance with other portions of the Matsuura publication in that the described process is related to the production of edible soybean products, which would have been known to require the removal of active soy trypsin inhibitory proteins. [See, for example, Matsuura, p. 6, ¶0007 and p. 8, ¶0010; Declaration of Katharine Martin, ¶¶4, 5]

Moreover, Matsuura does not distinguish among "whole soybeans", "dehulled soybeans" and "defatted soybeans", despite the fact that the process conditions to which dehulled and defatted soybeans are subjected denature soy trypsin inhibitor protein. Matsuura states that:

> …in the case where whole soybeans are used as a raw material, the same procedure for dehulled soybeans is applied except that the soaking time is made longer. In the case where this soaked liquid is concentrated, concentration under reduced pressure is carried out under the conditions of 45 to 65 °C and 600 to 700 mmHg in such a manner that the soluble sugar content is in the range of 10 to 50 g/100 ml. [Matsuura, p. 7, ¶0009].

Thus, Matsuura centers on producing extract that contains "soluble sugar" and is not concerned with producing extract that contains soy trypsin inhibitory proteins. Nowhere does Matsuura recognize or disclose that the extracts derived from dehulled or defatted soybeans should be carefully treated so as to avoid denaturing proteins therein. As set forth above, Matsuura indicates that even the soaked liquid derived from whole soybeans, when concentrated, is subjected to high temperature conditions.

In view of the foregoing discussion, appellants respectfully submit that claim 6 must be read in its entirety as well as in the context of the entire Matsuura text. Claim 6 clearly includes a heating step. Matsuura, therefore, does not ***inevitably*** lead one of ordinary skill in the art to the compositions set forth in appellants' invention.

e. The Soaking Liquid Described by Matsuura Does Not Inevitably Contain Soy Trypsin Inhibitor Protein

The Examiner's Answer further takes up the point that Matsuura states that "it is not the soybeans, but the liquid in which they have soaked which is the extract utilized in the composition of JP '442…" [Examiner's Answer, p. 7]. The Examiner's Answer contends that "…appellant's claims are drawn to a 'non-denatured soy extract' and the water extracted soybean composition of JP '442 does result in a non-denatured soy extract since soybeans are the starting material, they are extracted with water and then the water is the soybean extract." [Examiner's Answer, p. 7]

As set forth above and in the Declaration of Miri Seiberg of July 30, 2008, protein extraction by soaking whole soybeans in water is highly unlikely to result in obtaining active soy trypsin inhibitory protein in the soaking liquid. [Declaration of Miri Seiberg, July 30, 2008, ¶¶6, 7] Because protein molecules are so large, whether they are crystallized or not, it is difficult for them to move easily through cell walls and plant structures.

The Examiner's Answer further responds to appellants' argument that "…even in the instance in which there is a 'protein fraction' generated by a process, this protein fraction is precipitated out of the extract that is to be used in topical compositions [in Matsuura]" [Examiner's Answer, p. 7]. The Examiner's Answer asserts that:

> …Upon closer inspection of paragraph 11…it is clear that this is only done in the case where whey is generated as a by-product during the production of a soy protein isolate is used as a raw material. Claim 6 of JP '442 clearly does not require this. In fact claim 6 makes it very clear that no high heat is ever used and that the soybeans are crushed making it clear that water used as the solvent could easily release the STI and diffuse them into the extract. The STI of JP '442 and that of appellants is never crystallized as it is in Kunitz. [Examiner's Answer, p. 7].

The Examiner's Answer presumes that soy trypsin inhibitory proteins appear in the soaking liquid. Appellants have amply demonstrated that this assumption is inapposite. As set forth above, a heating step is presumed in accordance with the text of claim 6. The Matsuura publication is relied upon for its purported *inherent* disclosure of the compositions and methods of appellants' invention. Demonstrating inherency

"requires that the missing descriptive material is '*necessarily present*,' not merely probably or possibly present, in the prior art." *Trintec Industries, Inc. v. Top-U.S.A. Corporation*, 295 F.3d 1292, 1295 (Fed. Cir. 2002). (emphasis added)

The statement in claim 6 that filtration takes place after the ground soybean material is heated indicates that a heating step is taught. Temperatures for such a heating step range up to 100ºC, the higher temperatures of which would denature the soy trypsin inhibitory proteins therein. Thus, it cannot be said that the processes described in Matsuura would ***necessarily*** result in the compositions of appellants' invention.

f. The "Soy Milk" of Appellants' Compositions and Methods Contain Soy Trypsin Inhibitory Protein; The "Soy Milk" of Matsuura Does Not

The Examiner's Answer cites appellants' Specification indicating the understanding of soy trypsin inhibitor and contends that the mention of "soy milk" in that description implies that it is the same soybean extract as that described in Matsuura. Appellants respectfully submit that the compositions and methods of their invention require the presence of active soy trypsin inhibitor. The term "soy milk" is simply a description of the ***form*** of the soybean extract, which may or may not contain STI, depending upon the manner in which it is derived from the soybeans. As demonstrated above, the soybean extract of Matsuura would not ***necessarily*** contain active soy trypsin inhibitor protein. The methods and compositions of appellants' invention require the presence of active soy trypsin inhibitory activity [See, e.g., Claim 75 of the above-captioned patent application], which is different from the soy milk described in Matsuura. [Matsuura, p. 4, ¶0003] Mastsuura refers to soy milk as a "beverage" [Matsuura, p. 8, ¶0010], implying suitability for ingestion and lack of the presence of active soy trypsin inhibitory proteins.

iii. Conclusion

Accordingly, based on the reasons outlined above, the Appeal Brief and the Declarations submitted concurrently therewith, appellants respectfully submit that the Matsuura publication does not explicitly or inherently disclose, teach or suggest explicitly or inherently the subject matter of claims 75-84. Appellants therefore respectfully

request that the rejection of claims 75-84 under 35 U.S.C. 102(b) as being anticipated by the Matsuura publication be overruled.

Respectfully submitted,

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